Summary of Safety and Probable Benefit
CryoLife , Inc. BioGlue® Surgical Adhesive

A. General Information

Device Generic Name: ..... Surgical Adhesive

Device Trade Name: ..... BioGlue®® Surgical Adhesive (BioGlue®)

Applicant's Name and Address ..... CryoLife, Inc.
1655 Roberts Boulevard, NW
Kennesaw, Georgia 30144

Humanitarian Device Exemptions (HDE) Number: H990007

Date of HDE: ..... June 9, 1999

Date of Humanitarian Use Device Designation: ..... March 29, 1999

Date of Panel Recommendation: ..... Not Applicable (Refer to Section J for discussion)

Date of Notice of Approval to Applicant: ..... DEC 7 1999

B. Indications For Use

BioGlue Surgical Adhesive is intended to be used as an adjunct to the surgical repair of acute thoracic aortic dissections.

C. Device Description

BioGlue Surgical Adhesive (BioGlue®) is composed of purified bovine serum albumin (protein) and glutaraldehyde (crosslinking agent). These components come in a kit that includes a delivery system, applicator tips and extensions. The product's two components are mixed within the applicator tip of the delivery device during application to tissue. Polymerization of the surgical adhesive begins immediately upon mixing, reaching bonding strength within 2 minutes.

D. Contraindications, Warnings and Precautions

Contraindications

- Do not use in patients with known sensitivity to bovine products or glutaraldehyde.
- Not for use within true vessel lumen.
- Not for use as the sole treatment of dissecting thoracic aneurysm without sutures or staples. BioGlue® is to be used only adjunctively to facilitate surgical repair of thoracic aortic dissections by obliterating the false channels and strengthening the friable diseased aortic tissue for suture placement.

Warnings

- BioGlue® Surgical Adhesive solutions cartridges and applicator tips are for single patient use only. Do not re-sterilize.
  The delivery device may be reused and resterilized (reference section IX.D in Instructions for Use Maintaining Device Effectiveness).
- Do not expose tissue to the device if it may be adversely affected by contact with the device, e.g., aortic valve cusps and intracardiac structures.
- Do not allow device in either the uncured or polymerized form to contact blood flow.
- Avoid exposing nerves to the device, e.g., phrenic and recurrent laryngeal nerves.
- Avoid contact with skin or other tissue not intended for application.
- Glutaraldehyde treated tissue has an enhanced propensity for mineralization. Laboratory experiments indicate that glutaraldehyde may have mutagenic effects.
- Glutaraldehyde may cause irritation to eye, nose, throat, or skin, induce respiratory distress, and local tissue necrosis. Prolonged exposure to glutaraldehyde may cause a central nervous system or cardiac pathology. Operators using the device should ensure that staff are adequately risk protected.
- Exposure to bovine serum albumin may provoke an immune response, e.g., swelling or edema at the application site.
- BioGlue® Surgical Adhesive contains a material of animal origin, which therefore may be capable of transmitting infection.

Precautions

- It is recommended that surgical gloves, sterile gauze pads/towels and surgical instruments be maintained moist to minimize inadvertently polymerizing BioGlue® on these surfaces.
- Wear gloves, mask, protective clothing, and safety glasses. If contact with solution occurs, flush affected areas immediately with water and seek medical attention.
- Do not use if packages have been opened or damaged.
- Do not prime delivery device until ready for use. Premature priming may cause the applicator tip to become obstructed with polymerized adhesive.
- Use only sufficient adhesive to ensure desired obliteration of the dissection. Excessive material may adversely effect vessel compliance.

E. Adverse Effects of the Device on Health

The major causes of peri-operative morbidity and mortality associated with the standard surgical repair procedure for acute thoracic aortic dissections include cardiac tamponade, myocardial infarction, infection, hemorrhage, stroke, paraplegia, progressive dissection, and renal failure.[1,6,8,9,11,13]

CryoLife, Inc. has received no reports of BioGlue® related adverse events occurring outside of the United States in over 24 countries where it is commercially distributed. However, the following adverse events could potentially occur due to the composition of the device, the mode of application, and the disease process:

- Failure of product to adhere to tissue
- Application of adhesive to tissue not targeted for procedure
- Inflammatory, immune, or local and systemic allergic reaction

- Mineralization of tissue
- Local tissue necrosis
- Branch vessel obstruction
- Thrombosis and thromboembolism
- Possible transmission of infectious agents from material of animal origin

F. Alternative Practices and Procedures

A variety of surgical techniques are practiced in the United States for the surgical repair of acute thoracic aortic dissection. Generally dissections in the region of the entrance require prosthetic graft replacement. Pledgeted sutures are used to bolster the anastomosis between the native aorta and the graft. Hemostatic devices and/or pharmacological agents are commonly used to promote hemostasis during these procedures.

G. Marketing History

Commercial distribution of the device outside of the U.S. started in April 1998. Currently the device is marketed in the following countries: Argentina, Austria, Belgium, Bolivia, Denmark, Egypt, Finland, France, Germany, Greece, India, Ireland, Israel, Italy, Lebanon, The Netherlands, New Zealand, Norway, Portugal, South Africa, Spain, Switzerland, Syria, United Kingdom and Venezuela.

BioGlue® Surgical Adhesive has not been withdrawn from marketing for any reason relating to safety or probable benefit of the device.

H. Summary of Studies

1. Non-Clinical Studies

1.1 Biocompatibility

CryoLife conducted biocompatibility testing of BioGlue® Surgical Adhesive device implant material and all delivery system patient or adhesive solutions contacting materials in accordance with GLPs (good laboratory practices). All of the irradiated materials that come in contact with the BioGlue® adhesive solutions during storage were also assessed for extractables. The following table summarizes testing done on the glue components:

Table 1. Biocompatibility Testing Results-Glue Components

Test Performed	Extract(s)	Test and Control(s)	Results/Comments
Cytotoxicity (ISO)	MEM	Natural rubber (+) Silicone tubing (-)	L-929 cells gave a grade 2 (mild) reactivity score with test extract at 48 hours
Sensitization (Maximization)	Saline and CSO	Saline and CSO (-) DNCB (+) with and without activation	No sensitization was observed
Intracutaneous Toxicity (ISO/USP)	Saline and CSO	Saline and CSO	No toxicity observed in either extract
Systemic Toxicity (ISO/USP)	Saline (IV) and CSO (IP)	Saline and CSO	No signs of toxicity
Hemolysis (DHEW)	Saline	Saline (-) Water (+)	4.45% hemolysis, considered to be non-hemolytic
Rabbit pyrogen (ISO)	Saline	Saline (-)	<0.5 °C rise in all rabbits-non pyrogenic

Biocompatibility test results done on the applicator rip, cap housing, and cap plug included cytotoxicity, systemic and intracutaneous toxicity, sensitization, and pyrogenicity, and all passed/were non-toxic. There was also data in the file regarding the applicator rip connector extenders and extender tubing. These passed the cytotoxicity, sensitization, irritation/intracutaneous toxicity, and systemic toxicity tests.

CryoLife also evaluated BioGlue® Surgical Adhesive implant tissue response as part of a three month implant study to determine the effects of BioGlue®® Surgical Adhesive in the surgical repair of aortic dissection in sheep (see section 1.2.3 Animal Study Data). The observations of inflammation, necrosis, calcification and fibrosis in the BioGlue®-treated group were found to be consistent with a normal foreign body reaction.

Conclusions from the biocompatibility testing:

Based on these test results, the device materials suggest a biocompatible device.

1.2 Analytical and Functional Testing

Analytical and functional testing is conducted on each lot of BioGlue® Surgical Adhesive to ensure that it meets established product specifications designed to ensure the device is safe for its intended use. Analytical Tests include: UV-Vis Spectrophotometric Profile of Bovine Serum Albumin, pH Determination of Bovine Serum Albumin Solutions, Monomeric Content of Bovine Serum Albumin by SDS-PAGE, Protein Concentration of Bovine Serum Albumin Solutions by Colorimetric Assay, Glutaraldehyde Concentration Determination by Hydroxylamine-HCl Titration, and Extent of Autopolymerization of Glutaraldehyde by Absorbance Ratio. Functional tests include Adhesive Cure Rate and Adhesive Shear.

Conclusions from functional testing:

The device possesses adequate bonding strength, and is reproducible in its chemical characteristics.

1.3 Animal Study Data

A three-month study to determine the effects of BioGlue® in the surgical repair of aortic dissection in sheep was conducted to evaluate device performance in the repair of acute aortic dissection. This study

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involved use of a prototype device, the BG-2000, which utilized aseptically transferred solutions that had been sterilized by filtration and aseptically filled into the cartridges. The current BG-3000 device uses pre-filled cartridges that have been gamma irradiated. Additional animal studies employing the BG-3000 were not conducted because the results of *in vitro* testing of the BG-3000 suggested that the adhesive (shear strength) and monomeric impurity properties were not altered by the gamma irradiation.

A previously reported model of descending aortic dissection[2] was created in 30 sheep. After the aortic dissection was created, the surgeon determined if the dissection met the acceptance criteria established in the study protocol (i.e., a false lumen volume <50% of the total aortic volume, length of <7.1 cm and width < 2.6 cm). Dissections that did not meet these criteria were considered unstable for repair. Animals with acceptable dissections were then randomized in a blinded fashion to surgical repair of the proximal flap alone, or repair by gluing the layers of the dissection together with BioGlue® and surgical repair of the proximal flap. There were 26 aortic dissections that met the acceptance criteria, with 13 animals randomized to surgical repair alone and 13 to BioGlue® repair. The dissections varied in size from 5.0 to 7.0 cm long (average 5.2), 1.2 to 2.5 cm wide (average 1.4), encompassing 20-50% (average 35%) of the aortic volume. There were no statistical variations between the dimensions of the dissection in the surgical and BioGlue® groups.

In the BioGlue® group, four animals died of causes unrelated to the BioGlue® (3 pneumonia/weather stress, 1 tension pneumothorax immediately following surgery). In all four of these animals, the aortic dissection was completely obliterated or healed. In the 9 remaining BioGlue® animals, one animal died of chronic aortic aneurysm rupture at 51 days (due to mycotic super-infection of a technical glue failure) and in 8 animals surviving > 90 days the aortic dissection was completely healed (i.e. all of the layers of the aorta were fused and no false lumen or blind pouch observed) without signs of proximal or distal progression.

In the surgical control group, 1 animal died of pneumonia/weather stress. Four animals died within 24 hours of proximal or distal aneurysm progression and rupture. Eight animals survived 90 days. In 2 of the 8, the dissection healed after 3-3.5 cm of progression. In 2 of the 8, a chronic dissection formed at the surgical repair distal suture line and in 4 of the 8, a chronic dissection formed at re-entry points unrelated to the surgical repair site. In the chronic dissections, the false lumen made up 25-75% of the total aortic lumen. In all of the chronic dissections, the wall of the aorta was thinning and the diameter of the aorta was expanding, suggesting early aortic aneurysm formation.

Tissue response evaluations were also conducted, as noted above in section 1.1.

Conclusions from the animal studies:

Based on the results of this study, repair of aortic dissection using BioGlue® as an adjuvant to surgery in the sheep model was superior to surgery alone because:

- BioGlue® decreased the incidence of acute post-repair rupture of the aorta from 30% to 0%.
- BioGlue® decreased the incidence of re-dissection at the site of distal surgical repair from 17% to 0% in animals surviving 90 days.
- BioGlue® decreased the incidence of dissection progression prior to healing from 17% to 0% in animals surviving 90 days.
- BioGlue® decreased chronic dissection formation from 75% to 0% in animals surviving 90 days.

2. Clinical Studies

2.1 Introduction

The sponsor is currently conducting an Investigational Device Exemption (IDE) study (the BioGlue® Surgical Adhesive Effectiveness and Safety Trial, or "BEST" study) to assess the safety and effectiveness of the BioGlue® surgical adhesive used adjunctively in patients with Type A (ascending) thoracic aortic dissections. The study has a non-randomized Pilot Phase, and a randomized Phase II. The Pilot Phase involves enrolling 2 – 3 eligible patients at each of 20 centers, and began in June 1998. A total of 42 patients in the Pilot Phase of this study were followed acutely and data obtained is summarized in the sections below. Data are not yet available for the randomized Phase II part of the study.

2.2. Patient Selection

Eligibility criteria

The inclusion criteria for this study are:

- Male or Female patients at least 18 years of age.
- Patient has a confirmed diagnosis of an acute Type A aortic dissection and who, in the opinion of the Investigator, requires emergent surgical repair.
- Patient is willing and able to give written consent for the study. If the Patient is unconscious or under the influence of medications which render him or her unable to give fully informed consent, a guardian may provide informed consent for the patient regarding study participation.

The exclusion criteria for this study are:

- Patients with known hypersensitivity to albumin, bovine products, or glutaraldehyde.
- Patients who have been treated with an investigational product who have not completed the entire follow-up period.

2.3 Evaluation Criteria

Effectiveness Criteria

The criteria for evaluating clinical benefit in this patient population are:

- Reoperation of patients for bleeding or continued dissection.
- Ability of the BioGlue® to improve suturability of the friable dissected aorta.
- The need for additional hemostatic agents and pledgetted sutures.
- Intraoperative and early/hospital discharge mortality.
- Successful resuspension of aortic valve as measured by aortic insufficiency after surgical repair with the BioGlue® compared with preoperative value.
- Duration of surgery, defined as time from initial aortic cross-clamp (or initiation of deep hypothermic circulatory arrest, if performed first) until closure of the sternum.
- The durations of cardiopulmonary bypass, hypothermic circulatory arrest, aortic cross-clamp, and total operative time.

- The intraoperative blood products administered.
- The post-operative blood loss (chest tube drainage and blood replacement products).

Safety Endpoints

The criteria for evaluating safety in this patient population were:

- Unanticipated adverse device effects (UADE's).
- Device complications/malfunctions.
- Surgical procedure complications (adverse events).

2.4 Patient Population

Pertinent information about the patient population is tabulated below.

Table 2. Medical history.

	Number of Patients	Percentage of Patients
Hypertension	32	76.2%
Aortic Aneurysm	4	9.5%
Coronary Artery Disease	5	11.9%
Diabetes Mellitus IDDM – 0 NIDDM – 2	2	4.8%
Cardiac Tamponade	2	4.8%
Current Syncopal Episode	5	11.9%
Smoking History	18	42.9%
Current Stroke	1	2.4%
Ischemic or Dissection Induced Paralysis/Paraparesis	5	11.9%
Malperfusion Syndrome [§]	11	26.2%
Coronary	3	7.1%
Arch Vessel	2	4.8%
Thoracoabdominal	1	2.4%
Lower Extremity	4	9.5%
Upper Extremity	3	7.1%
Renal	1	2.4%

[§] Malperfusion Syndrome effected multiple locations in several patients.

Table 3. Etiology of aortic dissection.

Etiology	Number of Patients	Percentage of Patients
Medial Degeneration	8	19.0%
Atherosclerosis	5	11.9%
Arterial Hypertension	21	47.6%
Congenital Marfan's Disease – 1 Bicuspid Aortic Valve - 3	4	9.5%
Other Iatrogenic - 2 Medial Degeneration/ Hypertension - 1	3	11.9%

Table 4. Extent of the dissection.

Location of Distal Dissection	Number of Patients	Percentage of Patients
Ascending Aorta	9	21.4%
Aortic Arch	11	26.2%
Descending Aorta	8	19.0%
Aortic Bifurcation	4	9.5%
Iliofemoral	9	21.4%
Unknown	1	2.4%

Table 5. Concomitant procedures.

Procedure	Number of Patients	Percentage of Patients
Aortic Valve Replacement	8	19.0%
Coronary Artery Bypass Grafting CABG x 1 – 3 patients CABG x 2 – 2 patients	5	11.9%
Aortic Valve Resuspension	26	61.9%
Bentall Procedure	6	14.3%

Table 6. Adjunctive hemostatic agents used.

Surgical Adjuncts	Number of Patients	Percentage of Patients
Pledgets	25	60.5%
No Pledgets	13	39.5%
Pharmacological Hemostatic Agent	17	44.7%
Hemostatic Devices	8	21.1%
No Hemostatic Adjuncts	5	13.2%
No Hemostatic Devices	12	31.6%

Pharmacological hemostatic agents include: aprotinin, Factor IX, thrombin, and aminocaproic acid
Hemostatic devices include: Gelfoam, Surgicel, and Oxycel cotton

2.5 Safety Results

Mortality

Ten out of the 42 (23.8%) patients died perioperatively. No death was directly attributed to the use of the BioGlue®. All deaths were either within 30 postoperative days or prior to hospital discharge.

Table 7. Mortality summary.

Type of Death	Days to Death	Cause of Death
Intraoperative	0	Heart failure (unable to wean from cardiopulmonary bypass)
Early/Hospital Discharge	21	Diffuse subarachnoid and intraventricular hemorrhage
Early/Hospital Discharge	37	Multiple organ failure
Intraoperative	0	Probable cerebrovascular extension of dissection
Early/Hospital Discharge	2	Hyperkalemia secondary to rhabdomyolysis
Intraoperative	1	Cardiogenic shock from acute myocardial infarction
Early/Hospital Discharge	18	Heart failure
Intraoperative	1	Heart failure (unable to wean from cardiopulmonary bypass)
Early/Hospital Discharge	9	Progressive septicemia
Early/Hospital Discharge	1	Neurologic deficit/brain death

Reoperation

Ten of the 38 operation survivors (26.3%) had a reoperation. Two were for diffuse bleeding at the aortic dissection repair site; 2 for tamponade, 1 for ventilation dependency, 1 for respiratory failure, 2 to repair a femoral artery pseudoaneurysm at the cardiopulmonary bypass site, and 2 for delayed sternal closure. There were no reoperations for progression of the dissection. One patient suffered a cerebrovascular death intra-operatively, believed to be due to propagation of the dissection to involve arch vessels. An autopsy was not performed.

Post-operative Blood Loss

Table 8. Chest tube drainage.

	24 Hour Chest Tube Drainage (milliliters)	Total Drainage at Chest Tube Removal (milliliters)	Chest Tube Removal Time (hours)
N	38	37 [§]	37 [§]
Mean	1041	1510	62
Median	725	990.0	48
Std. Deviation	1060	1655	44
Minimum	0	0	15
Maximum	5300	7960	252

[§] Excludes one patient that died prior to chest tube removal.

Table 9. Adverse Events Incidence.

	Number of Patients	Percentage of Patients
Any Adverse Event	35	83.3%
Maximum Severity of Adverse Events:		
Mild	5	14.3%
Moderate	5	14.3%
Severe	13	37.1%
Life Threatening	12	34.3%
Serious Adverse Event (per protocol definition)	28	66.7%
Unanticipated Adverse Device Effects (UADE's)	-	-

Adverse Events/Serious Adverse Events (SAEs)

SAE [defined as an adverse event which meets one or more of the following criteria: 1) results in death, 2) is life-threatening, 3) requires in-patient hospitalization or prolongs hospitalization, 4) results in persistent or significant disability or incapacity] are tabulated below.

Table 10. Summary of adverse events by body system.

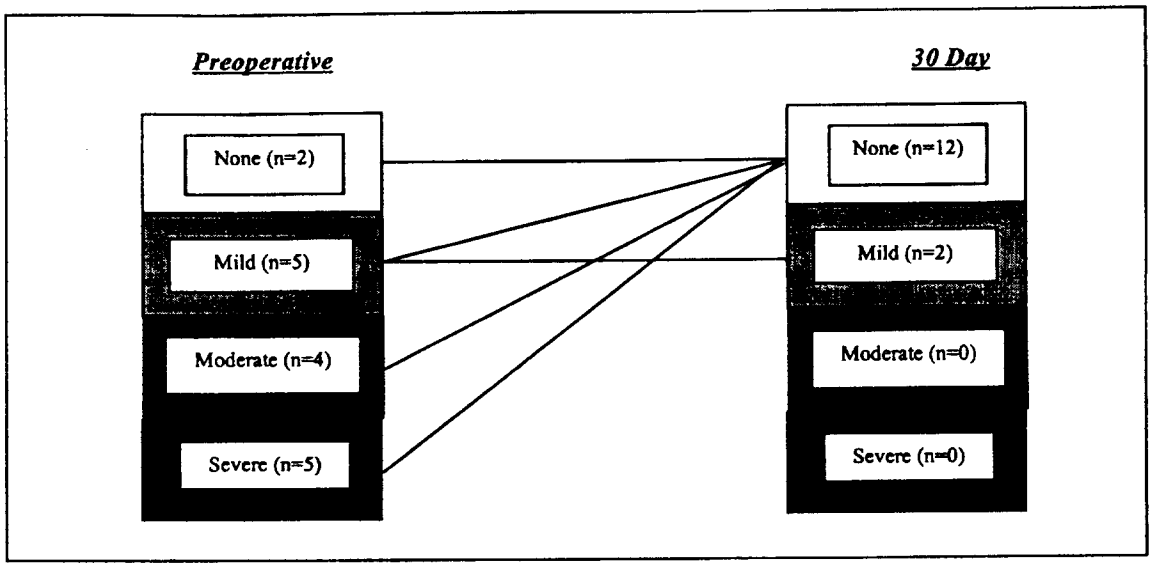
	Patients		Events
Body System	N	(%)	N
Body As A Whole	13	31.0	14
Cardiovascular	25	59.5	47
Digestive	3	7.1	3
Hepatic And Lymphatic	3	7.1	3
Metabolic And Nutritional	3	7.1	3
Nervous	7	16.7	7
Skin And Appendages	1	2.4	1
Special Sense	2	4.8	2
Urogenital	7	16.7	7

2.6 Probable Benefit Information

The tables and figures in this section present information from this feasibility study relating to probable benefit.

Twenty six patients had concomitant aortic valve resuspension at the time of the dissection repair surgery. Of these patients, 17 survived to the 30-day follow-up examination (the other nine patients died). The BioGlue® was used to adhere the ascending aorta at the valve sinuses in an attempt to preserve the native aortic valve. Figure 1 depicts changes in the aortic insufficiency in this group. In 20 patients (52.6%), no additional stitches ("make-up" stitches) were required after the interpositional graft replacing the ascending aorta was initially sutured in place.

Figure 1. Changes in aortic insufficiency in surviving patients undergoing aortic valve resuspension. Patients whose AI was not measured are excluded from this analysis.



Intraoperative Blood Products

Table11. Intraoperative blood products administered.

	Units of Intra-operative Red Blood Cells	Units of Intra-operative Cryoprecipitate	Units of Intra-operative Fresh Frozen Plasma	Units of Intra-operative Platelets	Total Units of Intra-operative Blood Products
N	36	35	37	37	37
Mean	2.5	6.4	3.7	6.3	18.5
Median	2	0	2	2	8
Std. Deviation	2.8	23.7	3.6	9.3	30.9
Minimum	0	0	0	0	0
Maximum	11	140	14	40	179

Figure 2. Quantity of intraoperative blood products.

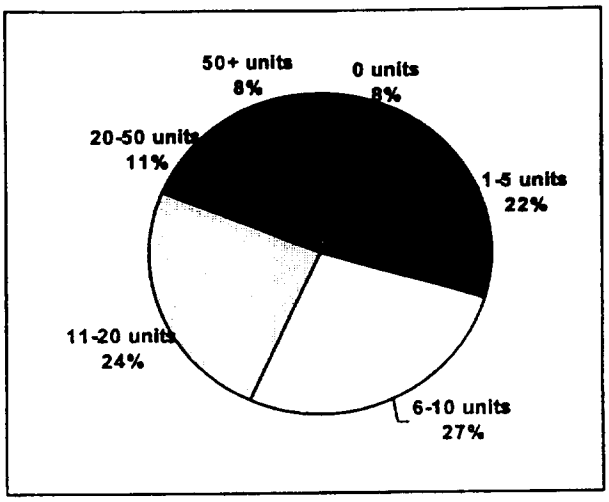


Table 12. Distribution of intraoperative blood products

Number of Total Units of Intraoperative Blood	Number of Patients [§]	Percentage of Patients
0	3	8.1%
1 – 5	8	21.6%
6 – 10	10	27.0%
11 – 20	9	24.3%
21 – 50	4	10.8%
50+	3	8.1%

[§] Intraoperative blood data was unknown for one patient.

2.7 Risk/Benefit Analysis

Probable Benefit

The classification of aortic dissection is determined by its location on the aorta. Based on the Stanford classification system[1], dissections are defined as follows:

- Type A – All dissections that involve the ascending aorta.
- Type B – Dissections limited to the descending aorta.

Dissections originating in the ascending aorta are considered to be the most lethal and are treated as surgical emergencies.

Aortic dissection has been reported to occur at a rate of 5-10 cases per million of population per year[2]. Within the United States, over 3,000 cases per year are reported[3]. Aortic dissection is 2-3 times more common in men than in women. Eighty percent of the patients presenting with this condition are hypertensive and over 40 years of age. Patients under 40 years of age typically have predisposing histories of Marfan's syndrome, coarctation of the aorta, or bicuspid aortic valves[4,5].

The purpose of surgical intervention for acute aortic dissection is to eliminate flow into the false lumen, and to reestablish blood flow to the normal aortic lumen.

The dissection renders the aortic tissue very friable, with high risk of further tearing and rupture after suture repair[7]. Despite the improvement in results of surgical repair of thoracic aortic dissections, the procedure is associated with considerable serious morbidity and mortality. These complications are directly related to duration of cardiopulmonary bypass, aortic cross-clamp, or hypothermic circulatory arrest. Much of the latter can be attributed to difficulties caused by the friable diseased tissue.

An analysis of the clinical results for 42 patients in the Lead-in phase of the "BEST" Study with Type A aortic dissections, failed to elicit AEs (adverse events) attributed to the BioGlue®, although 83% of the patients suffered an AE. This is consistent with the complexity of the surgery required for this life-threatening condition.

Safety

The AEs include cardiac tamponade, myocardial infarction, infection, hemorrhage, stroke, paraplegia, re-dissection, and renal failure. There were no unanticipated adverse device effects (UADEs) in this patient cohort.

"Lead-in" patients receiving the BioGlue® in the "BEST" study had an operative mortality of 9% and early/hospital discharge mortality rate of 23%. Figure 3 below depicts the preliminary performance of the BioGlue® compared to literature reported rates without adhesive.

Figure 3. Literature comparison of early/hospital mortality.

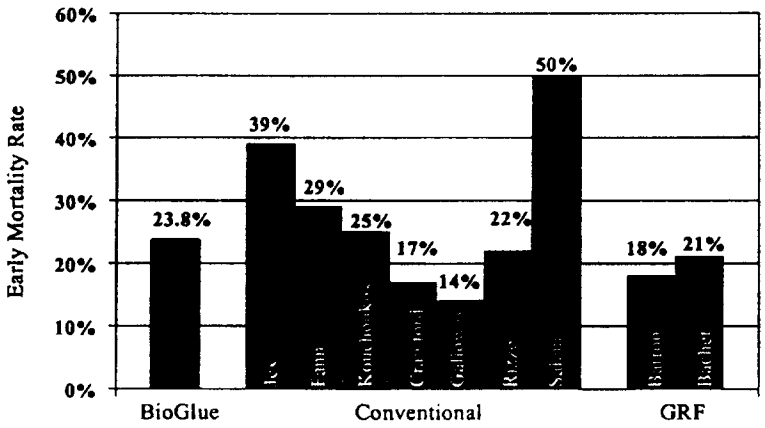


Figure 4. Literature comparison of hemorrhage-related mortality.

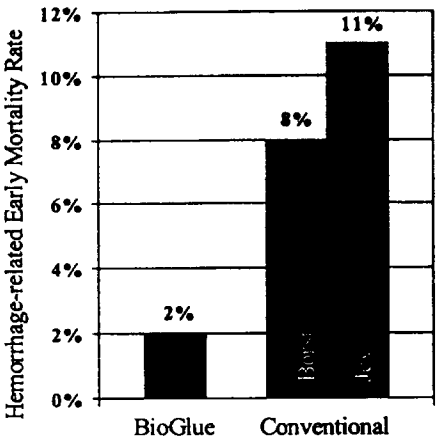


Figure 5. Literature comparison of hemorrhage-related reoperation.

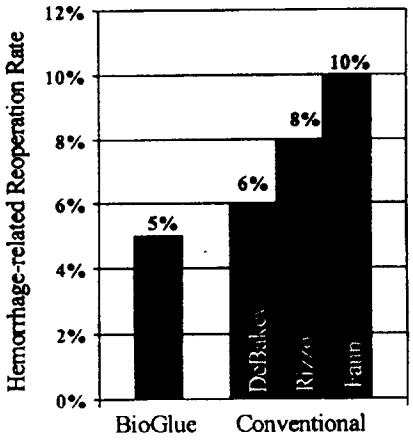
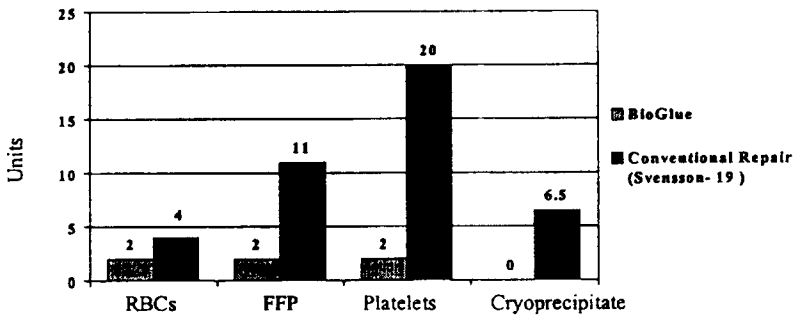


Figure 6. Literature comparison of median units of intraoperative blood products.



Conclusions from the clinical information

The data summarized previously in this section are based on the clinical results of an observational open study of 42 patients receiving the BioGlue® investigational device at 18 investigative sites. Control data submitted were derived from reports in the peer reviewed literature, both domestically and internationally. Data is suggestive of a benefit in terms of 1) decreased rate of reoperation for bleeding and other bleeding complications without the need for other hemostatic devices and/or pharmacological agents, 2) fewer intraoperative blood transfusions, and 3) reinforcement of friable tissue of the dissected aorta without the need for pledgets.

I. Conclusions Drawn From Studies

Biocompatibility testing of the patient contacting materials used in the device provides assurance of the biocompatibility of the BioGlue® Surgical Adhesive device. Clinical experience with the device and prototypes, together with analytical/functional testing and animal study data results, support its safety for the proposed intended use. Limited clinical data was available from a cohort of 42 patients enrolled in an IDE study at 18 investigative sites (BioGlue "BEST" IDE). This data, when compared to reports in the peer reviewed literature, suggest that the BioGlue® Surgical Adhesive device provides benefit without additional risks when used as an adjunctive to surgical treatment of acute thoracic aortic dissections.

The information provided in this HDE suggests that the BioGlue® Surgical Adhesive will not expose patients to unreasonable or significant risks of illness or injury, and that the probable benefit to health from use of the device outweighs the risk of injury or illness, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

J. Panel Recommendation

This HDE was not taken to an Advisory Panel because the adverse events of the surgery are available in the literature, and the adjunctive use of the surgical adhesive was not anticipated to result in adverse events that cannot be interpreted by the FDA.

K. CDRH Decision

CDRH has determined that, based on the data submitted in the HDE, the BioGlue® Surgical Adhesive will not expose patients to an unreasonable or significant risk of illness or injury, and the probable benefit to health from using the device outweighs the risks of injury or illness, and issued an approval order on DEC 7 1999. All facilities involved in the manufacture of this device have been inspected and found to be in compliance with the Quality System Regulation.

L. Approval Specifications

Directions for Use: See the Labeling (Attachment 1)

Warnings, Hazards to Health for use of the Device: See indications, contraindications, warnings, precautions and adverse effects in the Labeling (Attachment 1).

M. References

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